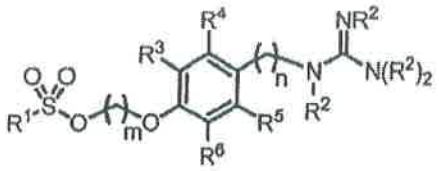
CLAIMS

1. A composition comprising a compound comprising formula (II):



(II),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, haloalkyl, alkynyl, alkenyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heterocyclyl, or heteroarylalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, -OR^7, -SR^7, -$N(R^7)_2$, or-$C(=O)R^8$, each optionally substituted;

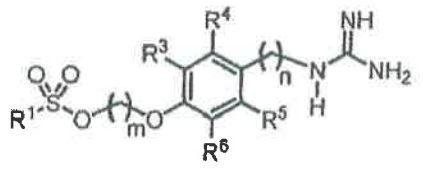
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, heterocyclyl, haloalkyl, aryl, or heteroaryl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, -OH, alkoxy, -NH_2, alkylamino, -SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

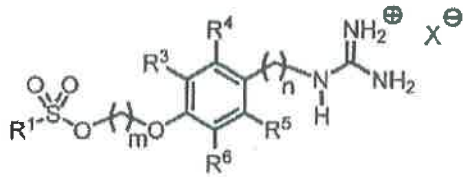
n is an integer between 1 and 4, inclusive.

2. A composition of claim 1, wherein the compound of formula (II) comprises the structure of formula (IV):



(IV),

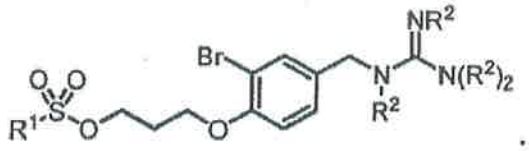
or a salt, free base, or combination thereof or the structure of formula (III):



(III),

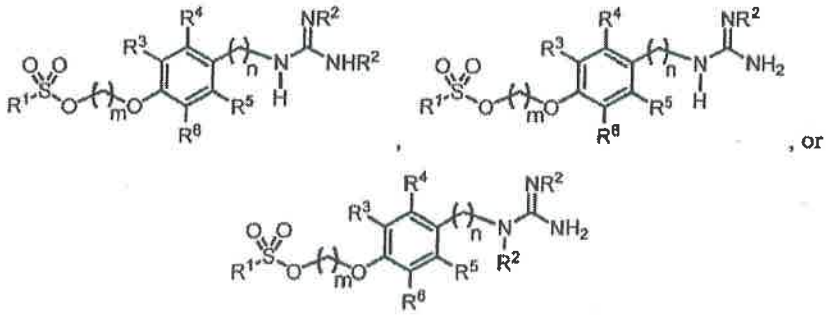
wherein $X^{\ominus}$ is a counter anion and wherein $X^{\ominus}$ is optionally halide, phosphate, sulfate, trifluoroacetate, tolunesulfonate, acetate, formate, citric, ascorbate, mesylate (methanesulfonate), or benzoate.

3. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



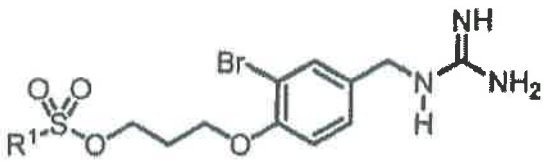
4. The composition of claim 1 or 3, wherein at least one R^2 is not hydrogen.

5. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

6. The composition of claim 1, wherein the compound of formula II comprises the formula:



or a salt, free base, or combination thereof.

7. The composition of any one of claims 1, 2, 4, and 5, wherein m is an integer between 1 and 10, inclusive; or between 1 and 8, inclusive; or between 1 and 6, inclusive; or 3, and optionally wherein n is 1.

8. The composition of any one of claims 1-7, wherein R^1 is:

(a) C_1-C_6 alkyl, haloalkyl, or aryl;

(b) methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *t*-butyl, pentyl, or hexyl;

(c) haloalkyl;

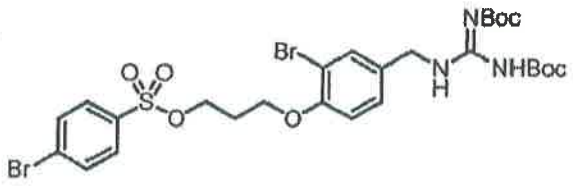
(d) CF_3;

(e) phenyl, optionally substituted; or

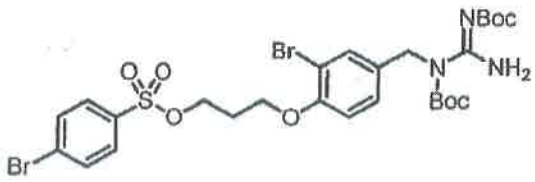
(f) 4-CH_3Ph, 2,4,6-$(CH_3)_3C_6H_2$, or C_6H_4X, wherein X is halide.

9. The composition of claim 1, wherein R^4, R^5, and R^6 are hydrogen; R^3 is halide or Br and the composition comprises a pharmaceutically acceptable salt of the compound of formula (II).

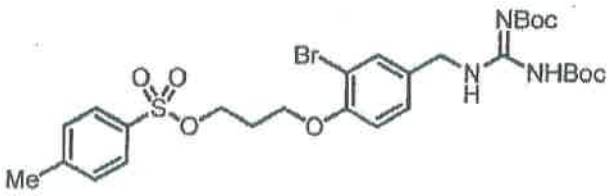
10. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



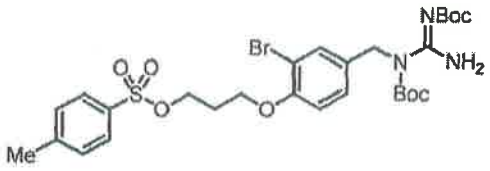
or a salt, free base, or combination thereof, or



or a salt, free base, or combination thereof, or



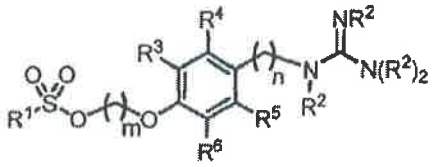
or a salt, free base, or combination thereof, or



or a salt, free base, or combination thereof.

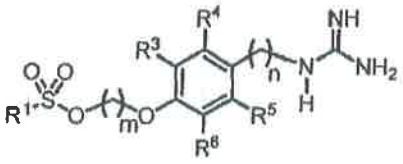
11. A method, comprising:

reacting a compound comprising formula (II):



(II)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (IV):



(IV),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, heterocyclyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group, provided at least one R^2 is not hydrogen;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, -OR^7, -SR^7, -$N(R^7)_2$, or-$C(=O)R^8$, each optionally substituted;

each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, -OH, alkoxy, -NH_2, alkylamine, -SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

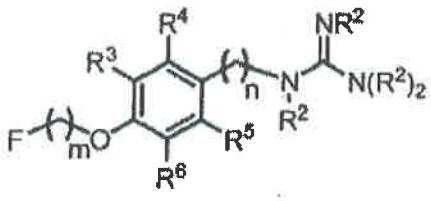
12. A method, comprising:

reacting a compound comprising formula (II):



(II)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (I):



(I),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heterocyclyl, heteroarylalkyl, alkenyl, alkynyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, -OR^7, -SR^7, -$N(R^7)_2$, or-$C(=O)R^8$, each optionally substituted;

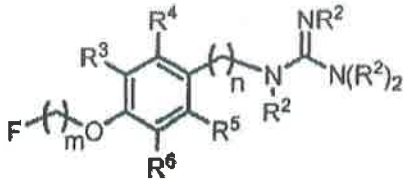
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, -OH, alkoxy, -NH_2, alkylamino, -SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

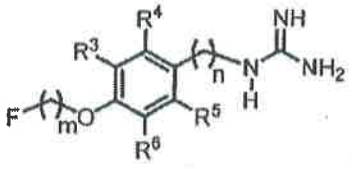
n is an integer between 1 and 4, inclusive.

13. A method of claim 12 further comprising reacting the compound comprising formula (I):



(I),

or a salt, free base, or combination thereof, provided at least one R^2 is not H, under conditions suitable to form a compound comprising formula (V):



(V),

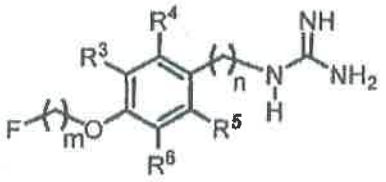
or a salt, free base, or combination thereof.

14. A method, comprising:
reacting a compound comprising formula (IV):



(IV)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (V):



(V),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, or haloalkyl, each optionally substituted;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, -OR^7, -SR^7, -$N(R^7)_2$, or-$C(=O)R^8$, each optionally substituted;

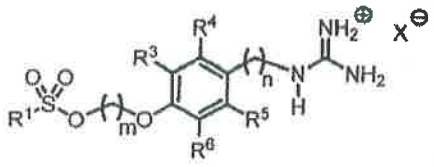
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, -OH, alkoxy, -NH_2, alkylamino, SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

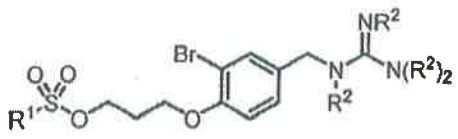
15. The method of claim 14, wherein the compound of formula (IV) comprises a compound of formula (III):



(III),

wherein $X^{\ominus}$ is a counter anion and wherein $X^{\ominus}$ is optionally halide, phosphate, sulfate, trifluoroacetate, tolunesulfonate, acetate, formate, citrate, ascorbate, mesylate (methanesulfonate), or benzoate.

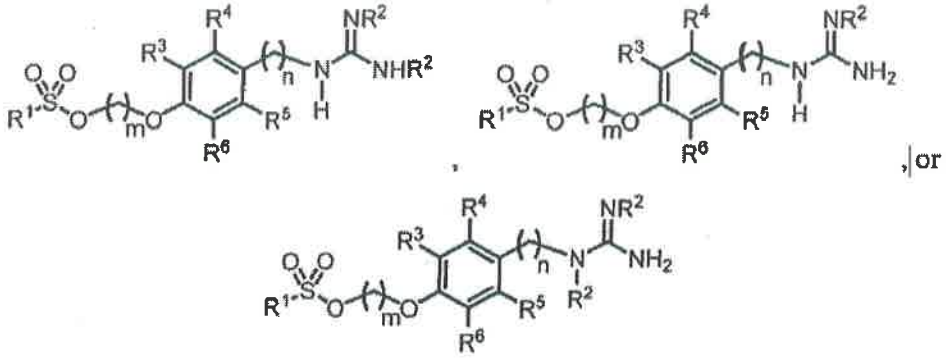
16. The method of claim 11 or 12, wherein the compound of formula (II) comprises a compound of formula:



or a salt, free base, or combination thereof.

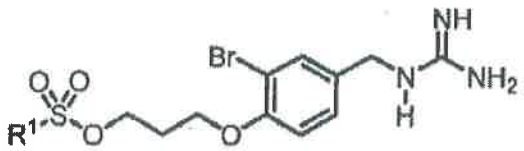
17. The method of any one of claims 11-13 and 16, wherein at least one R^2 is not hydrogen, optionally, wherein at least one R^2 is *t*-butyloxycarbonyl.

18. The method of any one of claims 11-13, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

19. The method of any one of claims 11-13, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

20. The method of any one of claims 11-15, and 18 , wherein m is an integer between 1 and 10 inclusive, or between 1 and 8 inclusive, or between 1 and 6 inclusive, or 3, and optionally wherein n is 1 and 3.

21. The method of any one of claims 11-20, wherein R^1 is:

(a) C_1-C_6 alkyl, haloalkyl, or aryl;

(b) methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *t*-butyl, pentyl, or hexyl;

(c) haloalkyl;

(d) R^1 is CF_3;

(e) phenyl, optionally substituted; or

(f) 4-$CH_3C_6H_4$, 2,4,6-$(CH_3)_3C_6H_2$, or C_6H_4X, wherein X is halide;

22. The method of claim 11 or 13, wherein the suitable conditions comprise exposing the compound of formula (I) and/or formula (II) to an acid, optionally wherein the acid is hydrochloric acid, formic acid, sulfuric acid, benzoic acid, acetic acid, trifluoroacetic acid, p-toluenesulfonic acid, phosphoric acid, or methanesulfonic acid.

23. The method of any one of claims 11-22, wherein the compound comprising formula (I), formula (II), and/or formula (IV) is provided as a solution in a solvent, optionally wherein the solvent is benzene, toluene, xylene, diethyl ether, glycol, hexane, pentane, methylene chloride, chloroform, dioxane, tetrahydrofuran, ethyl acetate, water, or mixtures thereof, and optionally wherein the suitable conditions comprise reacting at or above room temperature, optionally at a temperature of about 50°C, or about 60°C, or about 70°C, or about 80°C, or about 90°C, or about 100°C, or about 110°C, or about 120°C, or about 150°C, or about 170°C, or about 200°C, or about 225°C, or about 250°C for a period of about 5 minutes or less, or about 10 minutes or less, or about 20 minutes or less, or about 30 minutes or less.

24. The method of claim 12 or 14, wherein the suitable conditions comprise a solution pH of equal to or less than about 13, or equal to or less than about 12, or equal to or less than about 11, between about 8 and about 9, or between about 8 and about 10, or between about 7 and about 8.

25. The method of claim 11 or 13, wherein the suitable conditions comprise a solution pH equal to or less than 4, equal to or less than 3, equal to or less than 2, or equal to or less than 1.

26. The method of any one of claims 13-15 and 18-25, wherein the compound comprising formula (V) is isolated using column chromatography and optionally wherein the suitable conditions further comprise exposing a compound comprising Formula (II) or Formula (IV) to a source of fluoride in the presence of an ammonium salt or a bicarbonate salt, optionally wherein the molar ratio of ammonium salt or bicarbonate salt to the compound of formula (IV) is less than or equal to about 10:1, or less than or equal to about 9:1, or less than or equal to about 8:1, or less than or equal to about 7:1 or less than or equal to about 6:1, or less than or equal to about 5:1, or less than or equal to about 4:1, or less than or equal to about 3:1, or less than or equal to about 2:1, or less than or equal to about 1:1, optionally wherein the ammonium salt or the bicarbonate salt comprises the formula:

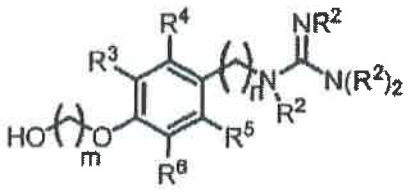
$$R_4NHCO_3$$

wherein R_4 is alkyl, or optionally wherein the bicarbonate salt is a tetraalkylammonium bicarbonate.

27. The method of any one of claims 12 and 14-26, wherein the step of reacting comprises exposing a compound comprising formula (II) or (IV) to a source of fluoride, optionally wherein the source of fluoride is isotopically enriched with ^{18}F.

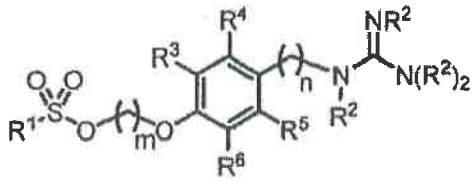
28. A method, comprising:

reacting a compound comprising formula (XI):



(XI)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (II):



(II),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, heterocyclyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group, provided at least one R^2 is not hydrogen;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, -OR^7 , -SR^7 , -$N(R^7)_2$, or-$C(=O)R^8$, each optionally substituted;

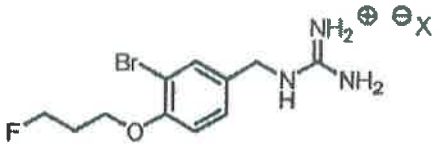
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, -OH, alkoxy, -NH_2, alkylamino, SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

29. A salt comprising formula (VI):



(VI)

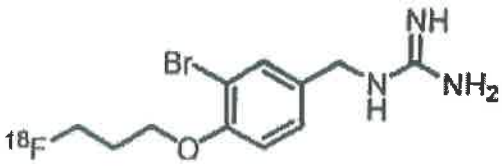
wherein $X^{\ominus}$ is formate or ascorbate, and optionally wherein the fluorine is isotopically enriched with ^{18}F.

30. A pharmaceutically acceptable composition comprising a salt of claim 29 and optionally a pharmaceutically acceptable excipient.

31. A method of imaging a subject, comprising:
administering a dose of a pharmaceutically acceptable composition of claim 30, and
acquiring at least one image of a portion of the subject.

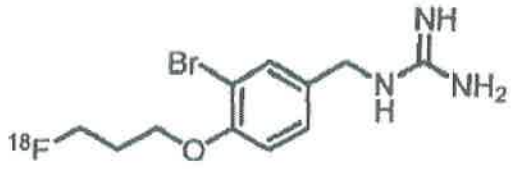
32. Use of a salt of claim 29 for imaging a portion of a subject.

33. A method of imaging a subject, comprising:
administering a dose of a compound comprising the formula:



or a free base, pharmaceutically acceptable salt, or combination thereof, to a subject,
wherein the maximum dose of the compound administered to the subject is approximately 15 mCi or less; and
acquiring at least one image of a portion of the subject.

34. A method for detecting norepinephrine transporter (NET) in a portion of a subject, the method comprising: administering a dose of a compound comprising the formula:



or a free base, pharmaceutically acceptable salt, or combination thereof, to a subject, wherein the maximum dose of the compound administered to the subject is less than approximately 14 mCi; and

acquiring at least one image of the portion of the subject, wherein the image detects NET in the subject, wherein the step of detecting comprises determining level, density, localization, and/or function of NET in the portion of the subject .

35. The method of claim 31, 33 or 34, wherein the maximum dose of the composition or compound administered to the subject is approximately 13 mCi or less, is between approximately 10 mCi and approximately 13 mCi, or is between approximately 8 mCi and approximately 10 mCi.

36. The method of any one of claims 31 and 33-35, wherein the portion of the subject being imaged is at least a portion of the cardiovascular system, or at least a portion of the tumor, or is at least a portion of the heart.

37. The method of any one of claims 31 and 33-35, further comprising determining the presence or absence of a cardiovascular disease or condition in the subject.

38. The method of any one of claims 31 and 33-36 further comprising:

administering a second dose of the compound to the subject at a time subsequent to the dose of claim 31 and 33-36; and

acquiring at least one image of the portion of the subject after the administration of the second dose of the compound and optionally further comprising:

comparing the at least one image acquired after the first dose with the at least one image acquired after the second dose; and

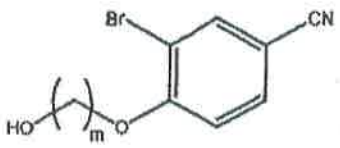
determining the presence or absence of differences between the cardiac sympathetic innervation at the time of administration of the first and second dose of the compound to the subject.

39. The method of claim 34, further comprising assessing cardiac sympathetic innervation in the subject.

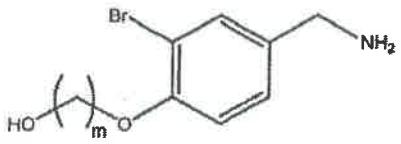
40. The method of claim 34, wherein image data from dynamic images are used to distinguish changes in local or global blood flow from changes in local or global NET function or distribution.

41. The method of claim 34, further comprising providing image data using another imaging agent, and determining blood flow based on the image data to distinguish local or global blood flow from local or global changes in NET function or distribution.

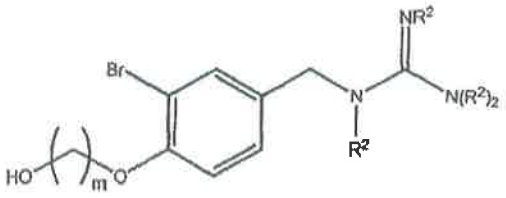
42. A compound comprising formula:



or a salt thereof, wherein m is an integer between 3 and 12, inclusive; or



or a salt, free base, or combination thereof, wherein m is an integer between 3 and 12, inclusive; or



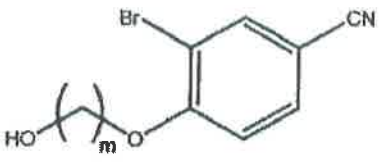
or a salt, free base, or combination thereof, wherein

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group; and

m is an integer between 3 and 12, inclusive.

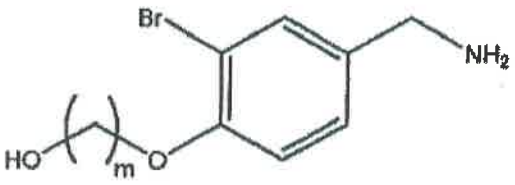
43. A method comprising:

reducing a compound comprising formula:



,

or a salt thereof, wherein m is an integer between 3 and 12, inclusive, with a reductant under suitable conditions to form a compound comprising:



,

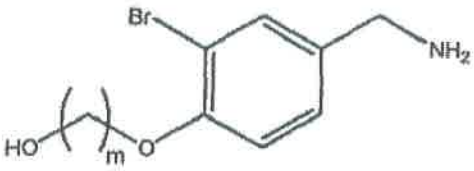
or a salt, free base, or combination thereof,

optionally, wherein m is 3; and

optionally, wherein the reductant is BH_3.

44. A method comprising:

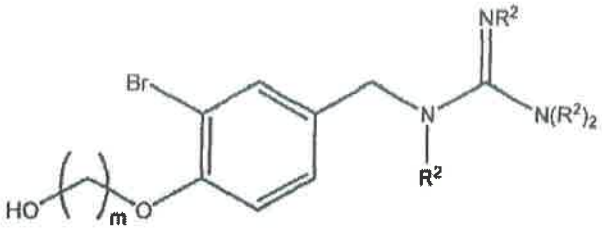
reacting a compound comprising formula:



,

or a salt, free base, or combination thereof, wherein

m is an integer between 3 and 12, inclusive; under conditions suitable to form a compound comprising formula:

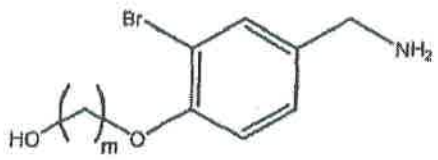


or a salt, free base, or combination thereof, wherein

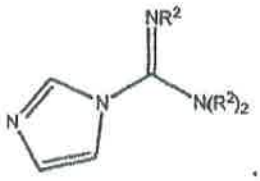
each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group; and

m is an integer between 3 and 12, inclusive, optionally, wherein m is 3; and

optionally wherein the step of reacting comprises reacting a compound comprising formula:



with a compound comprising formula:



45. A composition of claim 1, substantially as hereinbefore described with reference to any one of the Examples and/or Figures.

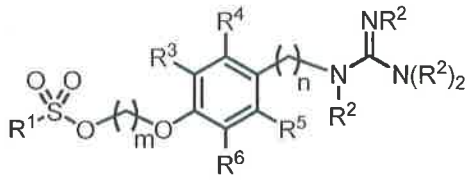
46. A method of any one of claims 11, 12, 14, 28, 33, 34, 43 and 44 substantially as hereinbefore described with reference to any one of the Examples and/or Figures.

47. A salt of claim 29, substantially as hereinbefore described with reference to any one of the Examples and/or Figures.

48. A compound of claim 42, substantially as hereinbefore described with reference to any one of the Examples and/or Figures.

Claims

1. A composition comprising a compound comprising formula (II):



(II),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, haloalkyl, alkynyl, alkenyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heterocyclyl, or heteroarylalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, $-OR^7$, $-SR^7$, $-N(R^7)_2$, or $-C(=O)R^8$, each optionally substituted;

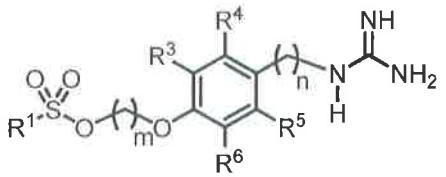
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, heterocyclyl, haloalkyl, aryl, or heteroaryl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, –OH, alkoxy, $–NH_2$, alkylamino, –SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

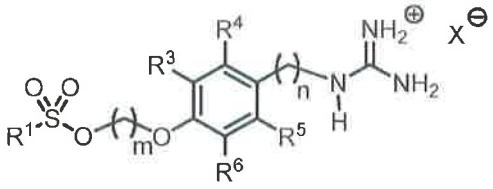
2. A composition of claim 1, wherein the compound of formula (II) comprises the structure of formula (IV):



(IV),

or a salt, free base, or combination thereof.

3. The composition of claim 2, wherein the compound of formula (IV) comprises formula (III):

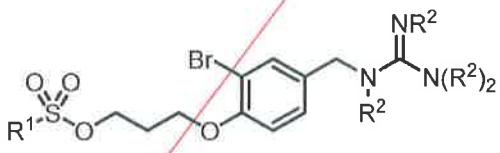


(III),

wherein $X^{\ominus}$ is a counter anion.

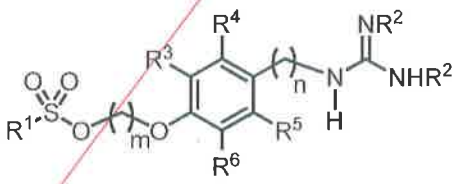
4. The composition of claim 3, wherein $X^{\ominus}$ is halide, phosphate, sulfate, trifluoroacetate, tolunesulfonate, acetate, formate, citric, ascorbate, mesylate (methanesulfonate), or benzoate.

5. The composition of claim 1, wherein the compound of formula (II) comprises the formula:

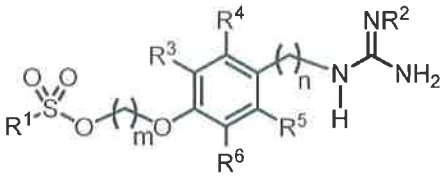


6. The composition of claim 1 or 5, wherein at least one R^2 is not hydrogen.

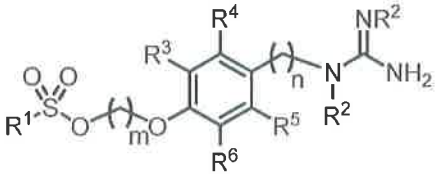
7. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



,

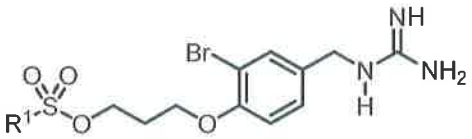


, or



or a salt, free base, or combination thereof.

8. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

9. The composition of any one of claims 1, 2, 3, 4, 6, and 7, wherein m is 3.

10. The composition of any one of claims 1, 2, 3, 4, 6, 7, and 9, wherein n is 1.

11. The composition of any one of claims 1, 2, 3, 4, 6, 7, 9, and 10, wherein R^3 is Br.

12. The composition of any one of claims 1-11, wherein R^1 is

(a) C_1-C_6 alkyl, haloalkyl, or aryl;

(b) methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *t*-butyl, pentyl, or hexyl;

(c) haloalkyl;

(d) CF_3;

(e) phenyl, optionally substituted; or

(f) 4-CH_3Ph, 2,4,6-$(CH_3)_3C_6H_2$, or C_6H_4X, wherein X is halide.

13. The composition of any one of claims 1-4, 6, 7, and 10-12, wherein m is an integer between 1 and 10, inclusive; or between 1 and 8, inclusive; or between 1 and 6, inclusive.

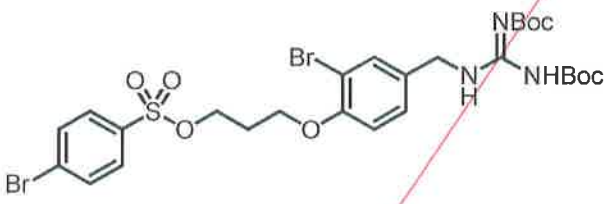
14. The composition of claim 1-3, wherein R^4, R^5, and R^6 are hydrogen; and R^3 is halide or Br.

15. The composition of claim 14, wherein the composition comprises a salt of the compound of formula (II).

16. The composition of claim 15, wherein the salt is a pharmaceutically acceptable salt.

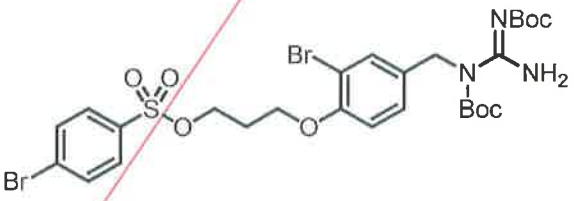
17. The composition of any one of claims 1, 5-7, and 9-16, wherein at least one R^2 is *t*-butyloxycarbonyl.

18. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



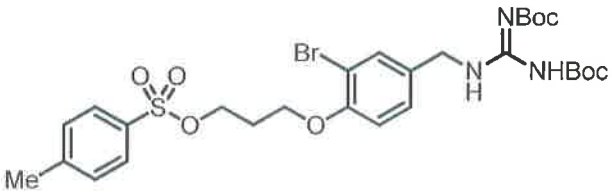
or a salt, free base, or combination thereof.

19. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



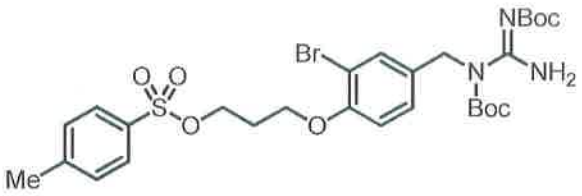
or a salt, free base, or combination thereof.

20. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

21. The composition of claim 1, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

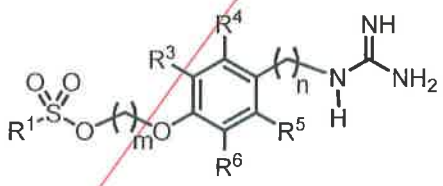
22. A method, comprising:

reacting a compound comprising formula (II):



(II)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (IV):



(IV),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, heterocyclyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group, provided at least one R^2 is not hydrogen;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, $-OR^7$, $-SR^7$, $-N(R^7)_2$, or $-C(=O)R^8$, each optionally substituted;

each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

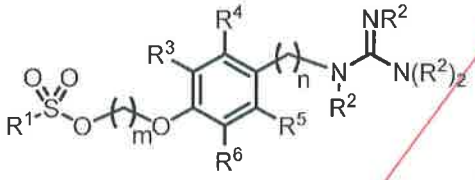
each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, –OH, alkoxy, $–NH_2$, alkylamino, –SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

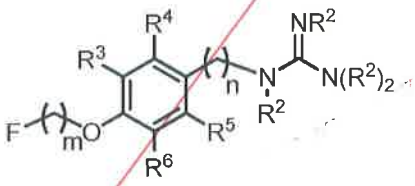
23. A method, comprising:

reacting a compound comprising formula (II):



(II)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (I):



(I),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heterocyclyl, heteroarylalkyl, alkenyl, alkynyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, $–OR^7$, $–SR^7$, $–N(R^7)_2$, or $–C(=O)R^8$, each optionally substituted;

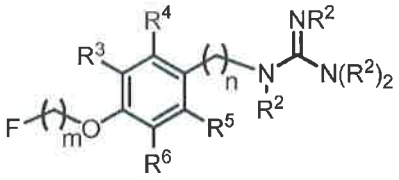
each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, –OH, alkoxy, $–NH_2$, alkylamino, –SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

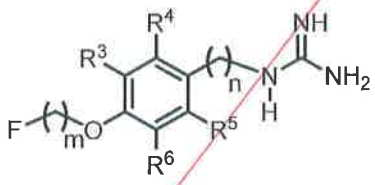
n is an integer between 1 and 4, inclusive.

24. A method of claim 23 further comprising reacting the compound comprising formula (I) :



(I),

or a salt, free base, or combination thereof, provided at least one R^2 is not H, under conditions suitable to form a compound comprising formula (V):

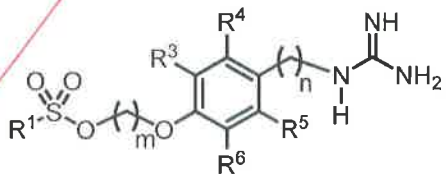


(V),

or a salt, free base, or combination thereof.

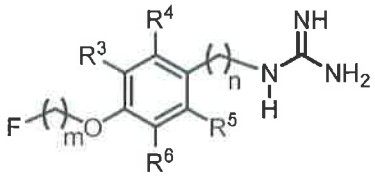
25. A method, comprising:

reacting a compound comprising formula (IV):



(IV)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (V):



(V),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, or haloalkyl, each optionally substituted;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, $-OR^7$, $-SR^7$, $-N(R^7)_2$, or $-C(=O)R^8$, each optionally substituted;

each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, –OH, alkoxy, $-NH_2$, alkylamino, –SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

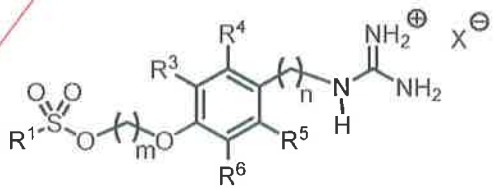
26. The method of claim 23, wherein the compound of formula (II) comprises a conpound of formula (IV):



(IV),

or a salt, free base, or combination thereof.

27. The method of claim 25 or 26, wherein the compound of formula (IV) comprises a compound of formula (III):

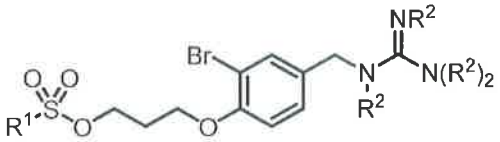


(III),

wherein $X^{\ominus}$ is a counter anion.

28. The method of claim 27, wherein $X^{\ominus}$ is halide, phosphate, sulfate, trifluoroacetate, tolunesulfonate, acetate, formate, citrate, ascorbate, mesylate (methanesulfonate), or benzoate.

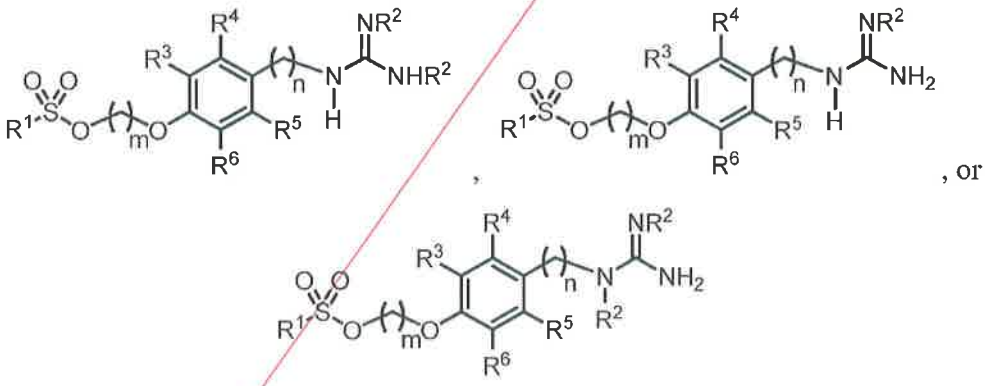
29. The method of claim 22 or 23, wherein the compound of formula (II) comprises a compound of formula:



or a salt, free base, or combination thereof.

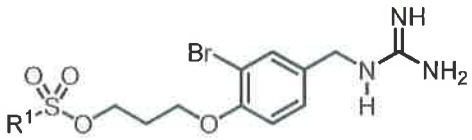
30. The method of any one of claims 22-24 and 29, wherein at least one R^2 is not hydrogen, optionally, wherein at least one R^2 is *t*-butyloxycarbonyl.

31. The method of any one of claims 22-24, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

32. The method of any one of claims 22-24, wherein the compound of formula (II) comprises the formula:



or a salt, free base, or combination thereof.

33. The method of any one of claims 22-28, 30, and 31, wherein m is 3.

34. The method of any one of claims 22-28, 30, 31, and 33, wherein R^3 is halide; and R^4-R^6 are hydrogen.

35. The method of any one of claims 22-28, 30, 31, 33, and 34, wherein R^3 is Br.

36. The method of any one of claims 22-35, wherein R^1 is:

(a) C_1-C_6 alkyl, haloalkyl, or aryl;

(b) methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *t*-butyl, pentyl, or hexyl;

(c) haloalkyl;

(d) R^1 is CF_3;

(e) phenyl, optionally substituted; or

(f) 4-$CH_3C_6H_4$, 2,4,6-$(CH_3)_3C_6H_2$, or C_6H_4X, wherein X is halide;

37. The method of any one of claims 22-28, 30, 31, and 33-36, wherein n is 1.

38. The method of any one of claim 22-28, 30, 31, and 34-37, wherein m is an integer between 1 and 10 inclusive, or between 1 and 8 inclusive, or between 1 and 6 inclusive.

39. The method of any one of claim 23-38, wherein F is isotopically enriched with ^{18}F.

40. The method of claim 22 or 24, wherein the suitable conditions comprise exposing the compound of formula (I) and/or formula (II) to an acid.

41. The method of claim 40, wherein the acid is hydrochloric acid, formic acid, sulfuric acid, benzoic acid, acetic acid, trifluoroacetic acid, p-toluenesulfonic acid, phosphoric acid, or methanesulfonic acid.

42. The method of any one of claims 22-41, wherein the compound comprising formula (I), formula (II), and/or formula (IV) is provided as a solution in a solvent.

43. The method of any one of claims 22-42, wherein the suitable conditions comprise reacting at or above room temperature.

44. The method of any one of claims 22-42, wherein the suitable conditions comprise reacting at a temperature of about 50 °C, or about 60 °C, or about 70 °C, or about 80 °C, or about 90 °C, or about 100 °C, or about 110 °C, or about 120 °C, or about 150 °C, or about 170 °C, or about 200 °C, or about 225 °C, or about 250 °C for a period of about 5 minutes or less, or about 10 minutes or less, or about 20 minutes or less, or about 30 minutes or less.

45. The method of claim 23 and 25, wherein the suitable conditions comprise a solution pH of equal to or less than about 13, or equal to or less than about 12, or equal to or less than about 11, between about 8 and about 9, or between about 8 and about 10, or between about 7 and about 8.

46. The method of claim 22 or 24, wherein the suitable conditions comprise a solution pH equal to or less than 4, equal to or less than 3, equal to or less than 2, or equal to or less than 1.

47. The method of any one of claims 22-45, wherein the solvent is benzene, toluene, xylene, diethyl ether, glycol, diethyl ether, hexane, pentane, methylene chloride, chloroform, dioxane, tetrahydrofuran, ethyl acetate, water, or mixtures thereof.

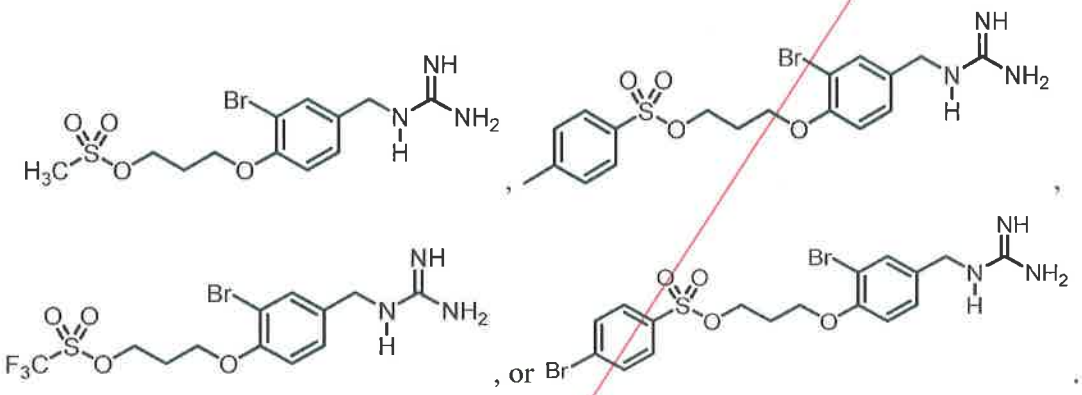
48. The method of any one of claims 24, 25, 27, 28, and 31-47, wherein the compound comprising formula (V) is isolated using column chromatography.

49. The method of any one of claims 23 and 25-48, wherein the step of reacting comprises exposing a compound comprising formula (II) or (IV) to a source of fluoride.

50. The method of claim 49, wherein the source of fluoride is isotopically enriched with ^{18}F.

51. The method of claim 49 or 50, wherein the source of fluoride is NaF or KF.

52. The method of any one of claims 22, 23, and 25-51, wherein a compound of formula (II) or (IV) comprises the structure:



53. The method of claim 48, wherein the suitable conditions further comprise exposing a compound comprising Formula (II) or Formula (IV) to a source of fluoride in the presence of an ammonium salt or a bicarbonate salt.

54. The method of claim 53, wherein the molar ratio of ammonium salt or bicarbonate salt to the compound of formula (IV) is less than or equal to about 10:1, or less than or equal to about 9:1, or less than or equal to about 8:1, or less than or equal to about 7:1 or less than or equal to about 6:1, or less than or equal to about 5:1, or less than or equal to about 4:1, or less than or equal to about 3:1, or less than or equal to about 2:1, or less than or equal to about 1:1

55. The method of claim 53 or 54, wherein the ammonium salt is an ammonium bicarbonate salt, ammonium hydroxide salt, ammonium acetate salt, ammonium lactate salt, ammonium trifluoroacetate salt, ammonium methanesulfonate salt, ammonium p-toluenesulfonate salt, ammonium nitrate salt, ammonium iodide salt, or ammonium bisulfate salt.

56. The method of claim 53 or 54, wherein the bicarbonate salt is a tetraalkylammonium bicarbonate.

57. The method of claim 53 or 54, wherein the ammonium salt or the bicarbonate salt comprises the formula:

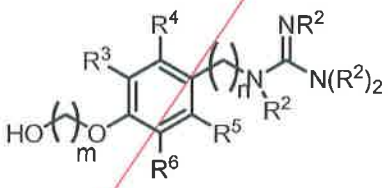
$$R_4NHCO_3,$$

wherein R_4 is alkyl.

58. The method of claim 23, wherein the reacting is carried out in the presence of a cryptand.

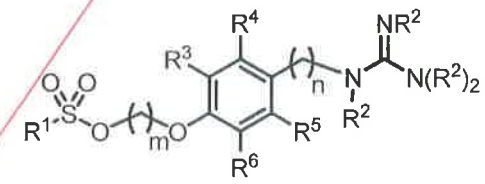
59. A method, comprising:

reacting a compound comprising formula (XI):



(XI)

or a salt, free base, or combination thereof, under conditions suitable to form a compound comprising formula (II):



(II),

or a salt, free base, or combination thereof, wherein:

R^1 is alkyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, heterocyclyl, or haloalkyl, each optionally substituted;

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group, provided at least one R^2 is not hydrogen;

R^3, R^4, R^5, and R^6 can be the same or different and are individually hydrogen, C_1-C_6 alkyl, heteroalkyl, halide, $-OR^7$, $-SR^7$, $-N(R^7)_2$, or $-C(=O)R^8$, each optionally substituted;

each R^7 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, or heterocyclyl, each optionally substituted;

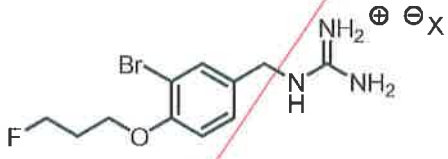
each R^8 can be the same or different and is hydrogen, alkyl, heteroalkyl, cycloalkyl, haloalkyl, heterocyclyl, aryl, heteroaryl, –OH, alkoxy, $–NH_2$, alkylamino, –SH, or alkylthiol, each optionally substituted;

m is an integer between 1 and 12, inclusive; and

n is an integer between 1 and 4, inclusive.

60. The method of claim 59, wherein the step of reacting comprises reacting the compound comprising formula (XI) with besylate chloride.

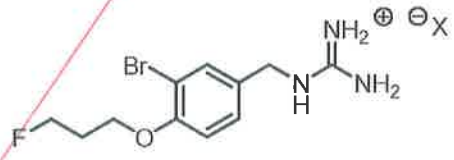
61. A salt comprising formula (VI):



(VI)

wherein $X^{\ominus}$ is formate.

62. A salt comprising formula (VII):



(VII)

wherein $X^{\ominus}$ is ascorbate.

63. The salt of claim 61 or 62, wherein the fluorine is isotopically enriched with ^{18}F.

64. A pharmaceutically acceptable composition comprising a salt of any one of claims 61-63, and optionally a pharmaceutically acceptable excipient.

65. A kit comprising a salt or composition of any one of claims 61-64 and instructions for use

66. A method of imaging a subject, comprising:

administering a dose of a pharmaceutically acceptable composition comprising a salt of claim 61-63, wherein the fluorine is optinally isotopically enriched with ^{18}F, and optionally a pharmaceutically acceptable excipient, to a subject; and

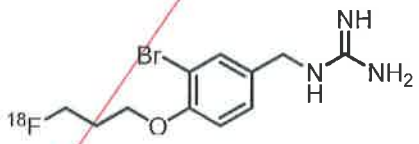
acquiring at least one image of a portion of the subject.

67. The method of claim 66, wherein the maximum dose of the salt is approximately 13 mCi or less.

68. Use of a salt of any one of claims 61-63 for imaging a portion of a subject.

69. A method of imaging a subject, comprising:

administering a dose of a compound comprising the formula:

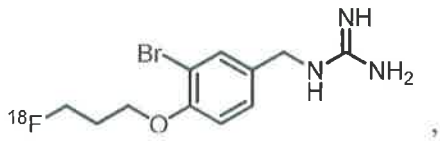


or a free base, pharmaceutically acceptable salt, or combination thereof, to a subject, wherein the maximum dose of the compound administered to the subject is approximately 15 mCi or less; and

acquiring at least one image of a portion of the subject.

70. A method for detecting norepinephrine transporter (NET) in a portion of a subject, the method comprising:

administering a dose of a compound comprising the formula:



or a free base, pharmaceutically acceptable salt, or combination thereof, to a subject, wherein the maximum dose of the compound administered to the subject is less than approximately 14 mCi; and

acquiring at least one image of the portion of the subject, wherein the image detects NET in the subject.

71. The method of claim 66, 69 or 70, wherein the maximum dose of the composition or compound administered to the subject is approximately 13 mCi or less, is between approximately 10 mCi and approximately 13 mCi, or is between approximately 8 mCi and approximately 10 mCi.

72. The method of any one of claims 66, 67, and 69-71, wherein the step of acquiring employs positron emission tomography.

73. The method of any one of claims 66, 67, and 69-72, wherein the portion of the subject being imaged is at least a portion of the cardiovascular system, or is at least a portion of the heart.

74. The method of any one of claims 66, 67, and 69-73, further comprising determining the presence or absence of a cardiovascular disease or condition in the subject.

75. The method of any one of claims 66, 67, and 69-74, wherein the composition or compound is provided for administration in a solution comprising between approximately 1% and approximately 10% ethanol and between approximately 25 mg/mL and approximately 75 mg/ml ascorbic acid.

76. The method of any one of claims 66, 67, 69, and 70 further comprising:

administering a second dose of the compound to the subject at a time subsequent to the dose of claim 66, 67, 69, or 70; and

acquiring at least one image of the portion of the subject after the administration of the second dose of the compound.

77. The method of claim 76 further comprising:

comparing the at least one image acquired after the first dose with the at least one image acquired after the second dose; and

determining the presence or absence of differences between the cardiac sympathetic innervation at the time of administration of the first and second dose of the compound to the subject.

78. The method of claim 70, wherein presence of NET indicates presence of a condition.

79. The method of any one of claims 69-78, wherein at least a portion of the compound is present as a pharmaceutically acceptable salt.

80. The method of claim 79, wherein the salt is a formate salt or the ascorbate salt of the compound.

81. The method of claim 70, wherein the step of detecting comprises determining level, density, localization, and/or function of NET in the portion of the subject.

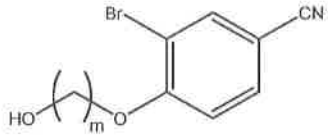
82. The method of claim 70 or 81, further comprising assessing cardiac sympathetic innervation in the subject.

83. The method of claim 70 or 81 wherein image data from dynamic images are used to distinguish changes in local or global blood flow from changes in local or global NET function or distribution.

84. The method of claim 70 or 81 further comprising providing image data using another imaging agent, and determining blood flow based on the image data to distinguish local or global blood flow from local or global changes in NET function or distribution

85. The method of claim 70, 83, or 84 further comprising assessing cardiac sympathetic innervation in the subject.

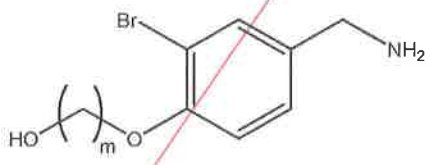
86. A compound comprising formula:



or a salt thereof, wherein m is an integer between 3 and 12, inclusive.

87. The compound of claim 86, wherein m is 3.

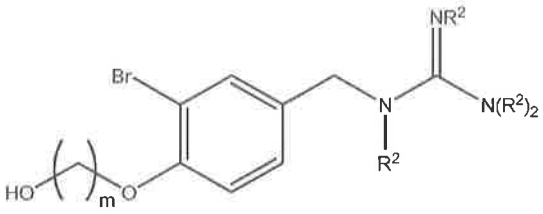
88. A compound comprising formula:



or a salt, free base, or combination thereof, wherein m is an integer between 3 and 12, inclusive.

89. The compound of claim 88, wherein m is 3.

90. A compound comprising formula:



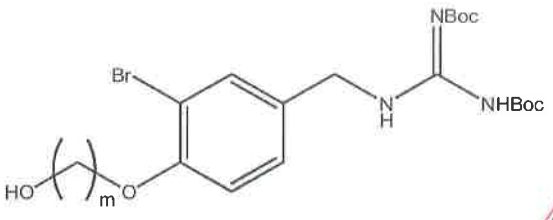
or a salt, free base, or combination thereof, wherein

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group; and

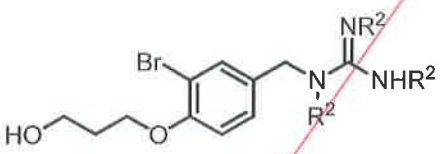
m is an integer between 3 and 12, inclusive.

91. The compound of claim 90, wherein m is 3.

92. The compound of claim 90 or 91 comprising formula:

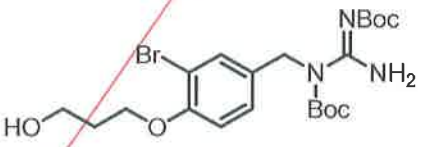


93. The compound of claim 90 comprising formula:



or a composition comprising the compound.

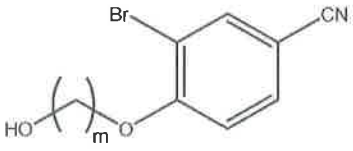
94. The compound of claim 90 comprising formula:



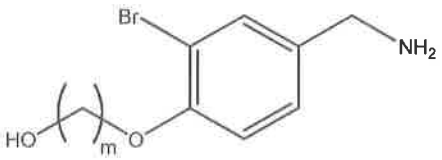
or a composition comprising the compound.

95. A method comprising:

reducing a compound comprising formula:



or a salt thereof, wherein m is an integer between 3 and 12, inclusive, with a reductant under suitable conditions to form a compound comprising:



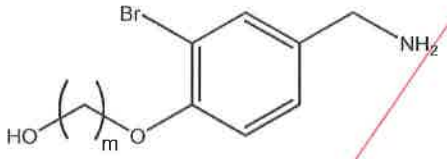
or a salt, free base, or combination thereof.

96. The method of claim 95, wherein m is 3.

97. The method of claim 95 or 96, wherein the reductant is BH_3.

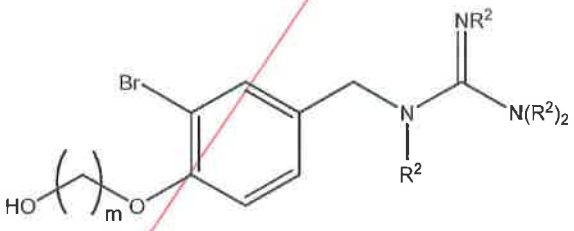
98. A method comprising:

reacting a compound comprising formula:



or a salt, free base, or combination thereof, wherein

m is an integer between 3 and 12, inclusive; under conditions suitable to form a compound comprising formula:



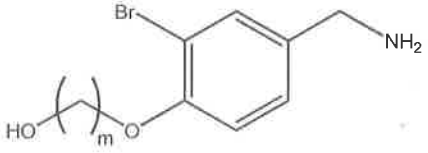
or a salt, free base, or combination thereof, wherein

each R^2 can be the same or different and is hydrogen or a nitrogen-protecting group; and

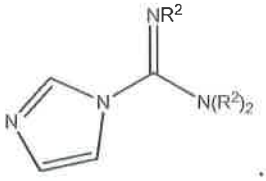
m is an integer between 3 and 12, inclusive.

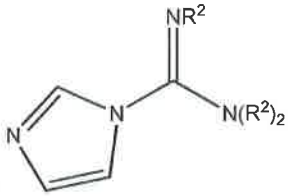
99. The method of claim 98, wherein m is 3.

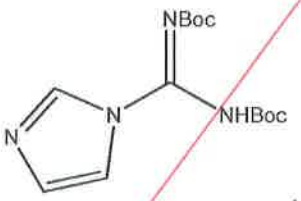
100. The method of claim 98 or 99, wherein the step of reacting comprises reacting a compound comprising formula:



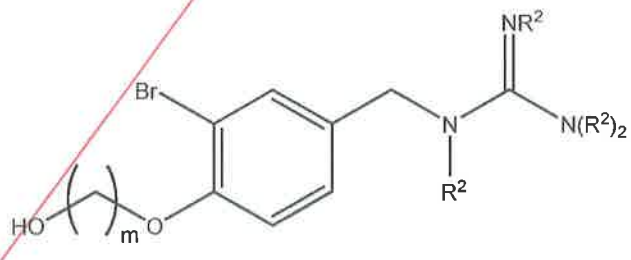
with a compound comprising formula:



101. The method of claim 98, 99, or 100, wherein the compound comprising formula:  is a compound comprising formula:



102. The method of claim 98, 99, 100, or 101, wherein the compound comprising formula:



is a compound comprsing formula:

